

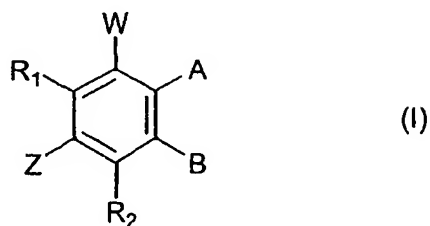
SUPPLEMENTAL PRELIMINARY AMENDMENT
U.S. Appln. No. 10/530,176

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

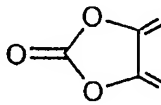
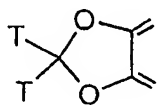
Claim 1. (Original) A method of increasing the sensitivity of cancer cells or a tumour to a chemotherapeutic agent by contacting said cells or tumour with an isoflavonoid compound of formula (I):



in which

R₁, R₂ and Z are independently hydrogen, hydroxy, OR₉, OC(O)R₁₀, OS(O)R₁₀, CHO, C(O)R₁₀, COOH, CO₂R₁₀, CONR₃R₄, alkyl, haloalkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, alkylaryl, alkoxyaryl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or

R₂ is as previously defined, and R₁ and Z taken together with the carbon atoms to which they are attached form a five-membered ring selected from



, or

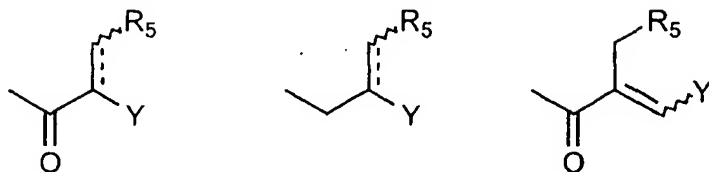
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R_1 is as previously defined, and R_2 and Z taken together with the carbon atoms to which they are attached form a five-membered ring selected from



and

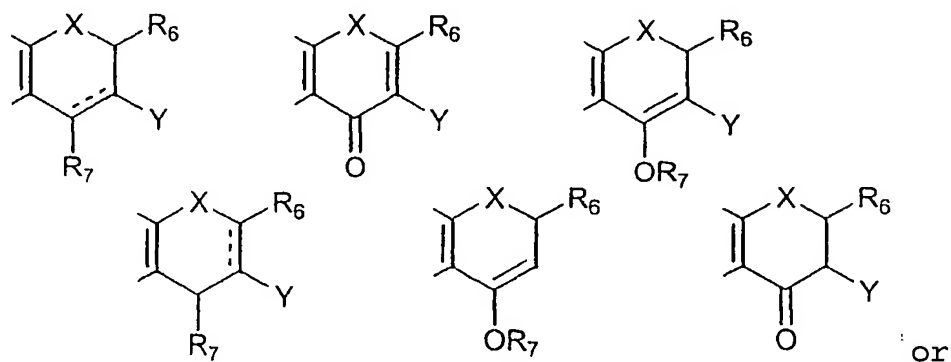
W is R_1 , A is hydrogen, hydroxy, NR_3R_4 or thio, and B is selected from



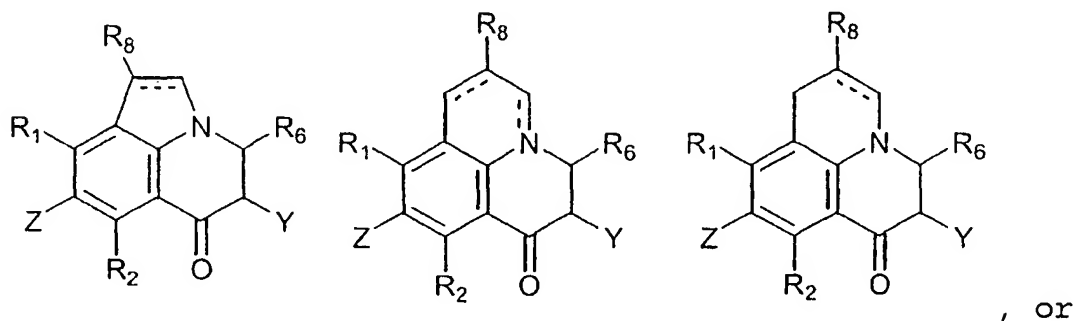
, or

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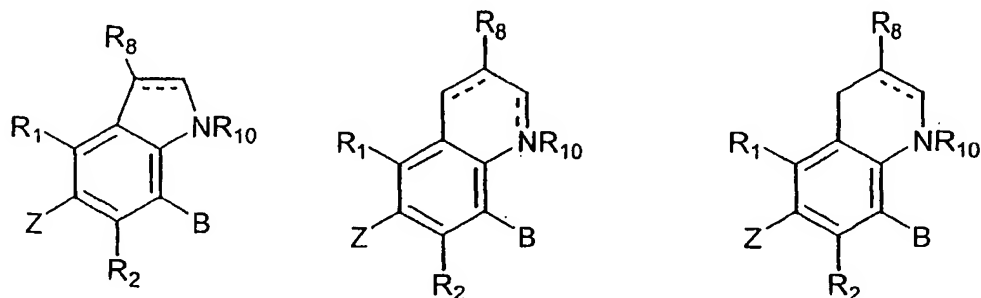
W is R₁, and A and B taken together with the carbon atoms to which they are attached form a six-membered ring selected from



W, A and B taken together with the groups to which they are associated are selected from

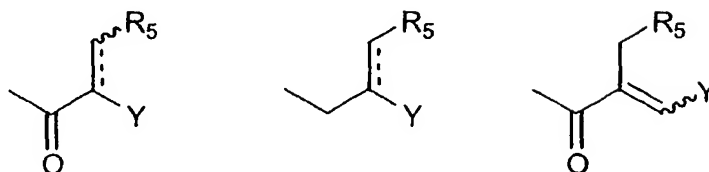


W and A taken together with the groups to which they are associated are selected from



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and B is selected from



wherein

R_3 is hydrogen, alkyl, arylalkyl, alkenyl, aryl, an amino acid, $C(O)R_{11}$ where R_{11} is hydrogen, alkyl, aryl, arylalkyl or an amino acid, or CO_2R_{12} where R_{12} is hydrogen, alkyl, haloalkyl, aryl or arylalkyl,

R_4 is hydrogen, alkyl or aryl, or

R_3 and R_4 taken together with the nitrogen to which they are attached comprise pyrrolidiny1 or piperidiny1,

R_5 is hydrogen, $C(O)R_{11}$ where R_{11} is as previously defined, or CO_2R_{12} where R_{12} is as previously defined,

R_6 is hydrogen, hydroxy, alkyl, aryl, amino, thio, NR_3R_4 , COR_{11} where R_{11} is as previously defined, CO_2R_{12} where R_{12} is as previously defined or $CONR_3R_4$,

R_7 is hydrogen, $C(O)R_{11}$ where R_{11} is as previously defined, alkyl, haloalkyl, alkenyl, aryl, arylalkyl or $Si(R_{13})_3$ where each R_{13} is independently hydrogen, alkyl or aryl,

R_8 is hydrogen, hydroxy, alkoxy or alkyl,

R_9 is alkyl, haloalkyl, aryl, arylalkyl, $C(O)R_{11}$ where R_{11} is as previously defined, or $Si(R_{13})_3$ where R_{13} is as previously defined,

R_{10} is hydrogen, alkyl, haloalkyl, amino, aryl, arylalkyl, an amino acid, alkylamino or dialkylamino,

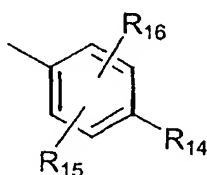
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the drawing "___" represents either a single bond or a double bond,

T is independently hydrogen, alkyl or aryl,

X is O, NR₄ or S, and

Y is



wherein

R₁₄, R₁₅ and R₁₆ are independently hydrogen, hydroxy, OR₉, OC(O)R₁₀, OS(O)R₁₀, CHO, C(O)R₁₀, COOH, CO₂R₁₀, CONR₃R₄, alkyl, haloalkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or any two of R₁₄, R₁₅ and R₁₆ are fused together to form a cyclic alkyl, aromatic or heteroaromatic structure, and pharmaceutically acceptable salts thereof.

Claim 2. (Original) A method of claim 1, wherein the sensitivity of the cancer cells or tumour to the chemotherapeutic agent is restored.

Claim 3. (Previously Presented) A method of claim 1, wherein the compound of formula (I) is administered to a subject in need of such treatment.

Claim 4. (Currently Amended) A combination therapy for the treatment, ~~or prophylaxis, amelioration, defence against and/or prevention~~ of cell proliferation, cancer or a disease associated with oxidant stress comprising administering to a subject a

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therapeutically effective amount of a compound of formula (\pm I) as defined in claim 1 and a chemotherapeutic agent.

Claim 5. (Cancelled).

Claim 6. (Currently Amended) A method of claim 54, wherein the cancer is selected from breast cancer, prostatic cancer, testicular cancer, ovarian cancer, uterine cancer, pancreatic cancer and colorectal cancer.

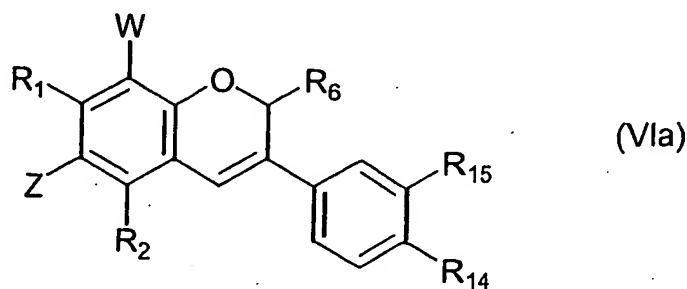
Claim 7. (Original) A method claim 6, wherein the cancer is selected from ovarian cancer, prostatic cancer and pancreatic cancer.

Claim 8. (Currently Amended) A method of claim 54, wherein the administration of the compound of formula (\pm I) precedes the administration of the chemotherapeutic agent.

Claim 9. (Currently Amended) A method of claim 54, wherein the administration of the compound of formula (I) and the chemotherapeutic agent is simultaneous.

Claim 10. (Currently Amended) A method claim 54, wherein the combination therapy follows observed resistance by cancer cells or tumour to a chemotherapeutic agent.

Claim 11. (Currently Amended) A method of claim 54, wherein the compound of formula (I) is an isoflav-3-ene of general formula (VIa):



wherein R_1 , R_2 , R_6 , R_{14} , R_{15} , W and Z are as defined in claim 1.

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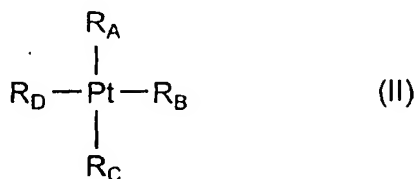
Claim 12. (Original) A method of claim 11, wherein the compound is dehydroequol.

Claim 13. (Currently Amended) A method of claim 54, wherein the chemotherapeutic agent is cisplatin, paclitaxel or ~~carboplatin~~ carboplatin.

Claim 14. (Cancelled).

Claim 15. (Currently Amended) A pharmaceutical ~~agent~~ composition comprising a compound of formula (I) of claim 1 and an anticancer agent.

Claim 16. (Currently Amended) A platinum-isoflavonoid complex or analogue thereof of the general formula (II):



in which

R_A , R_B , R_C , and R_D are independently halo, hydroxy, XR_E , alkoxy, $OC(O)R_F$, $OS(O)R_F$, thio, alkylthio, amino, alkylamino or dialkylamino,

X is O, NR_F or S, and

R_F is hydrogen, alkyl, arylalkyl, alkenyl, aryl or an amino acid,

wherein

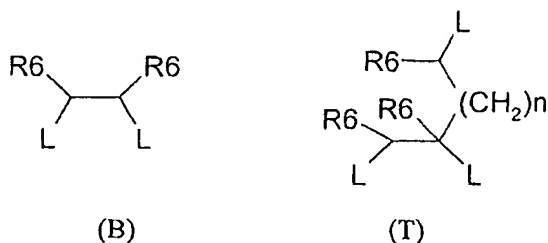
at least one of R_A , R_B , R_C , and R_D , and preferably only R_A , is XR_E where R_E is an isoflavonoid compound represented by general formula (I) ~~set out above~~ of claim 1 or is derived from or is a radical or ion of the isoflavonoid compound (I) and

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ligates to the platinum through any one or more of the heteroatoms X or a radical of the heteroatoms defined as part of R_E or alternatively by a double bond on the isoflavonoid compound (I)

and

when R_A is XR_E , R_B , R_C and/or R_D together may form part of a bidentate or tridentate ligand of general formulae (B) and (T) respectively



wherein L represents a ligating atom chosen from N, O and S, n is from 0 to 8, and

each R_6 is independently as defined above or may together form part of a cyclic alkyl, aromatic or heteroaromatic structure,

which platinum-isoflavonoid complexes include pharmaceutically acceptable salts thereof.

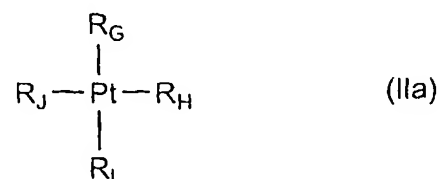
Claim 17. (Currently Amended) A method for the treatment, ~~or prophylaxis, amelioration, defence against, and/or prevention~~ of cell proliferation, cancer or a disease associated with oxidant stress which method comprises administering to a subject a therapeutically effective amount of one or more platinum-iosoflavanoid complexes of the formula (II) ~~as defined above of claim 16.~~

Claim 18. (Cancelled).

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Claim 19. (Currently Amended) A pharmaceutical composition comprising one or more platinum-isoflavonoid complexes of the formula (II) of claim 16 in association with one or more pharmaceutical carriers and/or excipients.

Claim 20. (Original) A composition comprising a platinum complex of the general formula (IIa),



in which

R_G , R_H , R_I , and R_J are independently halo, hydroxy, alkoxy, $OC(O)R_K$, $OS(O)R_K$, thio, alkylthio, amino, alkylamino or dialkylamino,

X is O, NR_K or S, and

R_K is hydrogen, alkyl, arylalkyl, alkenyl, aryl or an amino acid,

in association with an isoflavonoid compound of general formula (I) as defined in claim 1 and pharmaceutically acceptable salts thereof.

Claim 21. (Currently Amended) A method for the treatment, ~~or prophylaxis, amelioration, defence against, and/or prevention~~ of cell proliferation, cancer or a disease associated with oxidant stress which comprises administering to a subject a therapeutically effective amount of a composition of claim 20.

Claim 22. (Cancelled).

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Claim 23. (New) A pharmaceutical composition comprising a compound of formula (I) of claim 1 and a chemotherapeutic agent.

Claim 24. (New) The pharmaceutical composition of claim 23, wherein said chemotherapeutic agent is cisplatin, paclitaxel or carboplatin.

Claim 25. (New) The pharmaceutical composition of claim 1, wherein the compound is dehydroequol.